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Efficient and Selective Oxidation of Aromatic Amines to Azoxy Derivatives over Aluminium and Gallium Oxide Catalysts with Nanorod Morphology

Bhawan Singh,[a, b, c] Dalmo Mandelli,[c] and Paolo P. Pescarmona*[a]

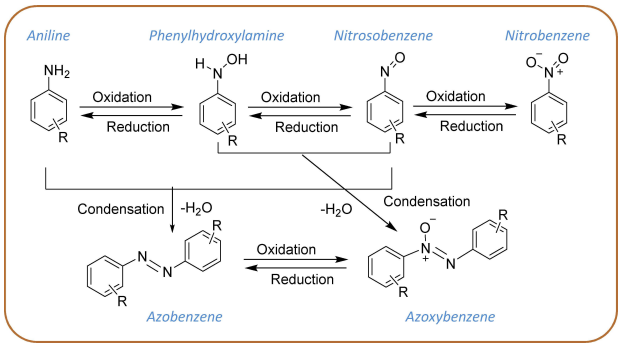
Aluminium oxide and gallium oxide nanorods were identified as highly efficient heterogeneous catalysts for the selective oxidation of aromatic amines to azoxy compounds using hydrogen peroxide as environmentally friendly oxidant. This is the first report of the selective oxidation of aromatic amines to their azoxy derivatives without using transition metal catalysts. Among the tested transition-metal-free oxides, gallium oxide nanorods with small dimensions (9–52 nm length and 3–5 nm width) and fully accessible, high surface area (225 $m^2 g^{-1}$) displayed the best catalytic performance in terms of substrate versatility, activity and azoxybenzene selectivity. Furthermore, the catalyst loading, hydrogen peroxide type (aqueous or anhydrous), and the amount of solvent were tuned to optimise the catalytic performance, which allowed reaching almost full selectivity (98%) towards azoxybenzene at high aniline conversion (94%). Reusability tests showed that the gallium oxide nanorod catalyst can be recycled in consecutive runs with complete retention of the original activity and selectivity.

1. Introduction

The selective oxidation of aromatic amines into O-containing derivatives such as hydroxylamine, nitroso, nitro, oxime, azo and azoxy compounds by using a sustainable chemical process has a great fundamental as well as practical interest.[1–4] Among this class of products, azoxy compounds have received considerable research attention owing to their versatile applications as dyes and pigments, reducing agents, analytical reagents, food additives, chemical stabilisers and polymer inhibitors.[5–9] In addition, azoxy compounds are used as precursors for Wallach rearrangement, which offers a straightforward path for the synthesis of azo compounds with one aromatic ring substituted with a hydroxyl group in *para*-position.[10,11] Moreover, some derivatives of azoxy compounds containing both aryl and alkyl groups are used in liquid crystal displays[12] and therapeutic drugs.[13,14]

Conventionally, azoxy compounds are synthesised either from the oxidation of amines or from the reduction of nitro compounds. In both cases, the formation of the azoxy derivatives is accomplished through the condensation of intermediate reaction products (Scheme 1). Due to the possible formation of different reaction products, it is quite challenging to control the reaction towards the selective formation of the azoxy product. Additionally, mild reaction conditions (i.e. low temperature and atmospheric pressure) and the use of green solvents and oxidants or reductants are preferable. For this purpose, the identification of an efficient and reusable catalyst is of the utmost importance.

Until now, numerous transition-metal-based homogeneous and heterogeneous catalysts have been developed for the selective oxidation of amines into azoxy compounds by using H_2O_2 or *tert*-butyl hydrogen peroxide (TBHP) as the oxidant. Homogeneous catalysts based on transition metals, such as tetrastearyl tetratitanate,[15] ruthenium chloride,[16] and



Scheme 1. Reaction pathways involved in the synthesis of azoxy compounds

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polyoxometalates[17] have been reported to be active and selective in the oxidation of aromatic amines into azoxy compounds. Recently, the reaction could be achieved also with 2,2,2-trifluoroacetophenone as organo-catalyst using hydrogen peroxide as the oxidant.[18] However, all these homogeneous systems suffer from the difficult separability and reusability of the catalyst. In order to overcome this issue, a variety of transition-metal-based heterogeneous catalysts including microporous and mesoporous titanosilicates (e.g. TS-1, Ti-Beta, Ti-ZSM-48, Ti-MCM-41, Ti-HMS, ETS-10, Ti-PILC),[3,19–23] transition metal oxides (such as TiO_2,[24,25] $LiNbO_3$,[26] $CuCr_2O_3$ spinel[27] and mesoporous CoO-SiO_2[28]) and supported metal or metal oxide nanoparticles (such as Ag on WO_3,[29] Ag on Fe_2O_3,[30] MnO_2 on graphene oxide[31] and Cu on CeO_2[32]) have been employed for the oxidation of aromatic amines into azoxybenzene derivatives. Although all these heterogeneous catalytic systems are active in the selective oxidation of amines to azoxy derivatives, they still suffer from one or more drawbacks, such as the use of expensive transition metals that may be prone to leaching, diffusion limitations, complex and tedious catalyst synthesis, inefficient recyclability and the use of high loading of catalyst. In this respect, the development of an efficient, transition-metal-free heterogeneous catalyst that can operate with an environmentally benign oxidant as H_2O_2 in the selective oxidation of aromatic amines to azoxy derivatives is an attractive and timely goal.

A class of transition-metal-free heterogeneous catalysts that has attracted research interest for the selective oxidation of unsaturated compounds to the corresponding epoxides in the last two decades consists of materials containing Ga or Al active sites, either as oxides (Al_2O_3 or Ga_2O_3)[33–36] or as metallosilicates (Ga-MCM-41, Al-MCM-41).[37,38] These catalysts operate with hydrogen peroxide as an environmentally friendly oxidant under relatively mild reaction conditions. In addition, they also have shown to be active and selective catalysts towards the formation of alkyl lactates from triose sugars.[39] Recently, our group discovered a template-free method to prepare Al_2O_3 and Ga_2O_3 nanorods (NR) with high specific surface area and a high population of accessible acid sites that act as catalytic sites for activating hydrogen peroxide.[36,40] Here, we report for the first time the catalytic performance of these aluminium and gallium oxides as heterogeneous catalysts for the selective oxidation of aromatic amines to azoxy derivatives with hydrogen peroxide as the oxidant. We reasoned that Al_2O_3-NR and Ga_2O_3-NR could be suitable catalysts for this reaction not only owing to their ability to activate hydrogen peroxide but also because their acid sites could catalyse the condensation of the phenhydroxylamine and nitrosobenzene intermediates leading to the formation of azoxybenzene (Scheme 1). The observed promising activity of these catalysts was further optimised by screening and tuning (i) the catalyst loading, (ii) the hydrogen peroxide source (aqueous or anhydrous), and (iii) the use and amount of solvent. For the optimum catalysts identified in this work (Ga_2O_3-NR), the versatility in the conversion of different substituted anilines and the reusability were demonstrated.

2. Results and Discussion

Recent reports showed that aluminium oxide and gallium oxide with nanorod morphology are highly active, selective and stable heterogeneous catalysts that are able to activate hydrogen peroxide towards the epoxidation of alkenes.[36,40] This feature has the potential to be exploited in other oxidation reactions involving the activation of hydrogen peroxide. In this context, we studied a set of Al and Ga oxides with different morphologies and crystal structures as transition-metal-free heterogeneous catalysts for the oxidation of aromatic amines to azoxy derivatives using hydrogen peroxide as an environmentally friendly oxidant. Al_2O_3 and Ga_2O_3 nanorods were prepared according to an organic-template-free protocol developed by our group and their catalytic performance was compared to the two most common polymorphs of gallium oxide, i.e. γ-Ga_2O_3 (surface area: 155 m^2/g, see Figure S1 for X-ray diffraction and N_2-physisorption data) and β-Ga_2O_3 (surface area: 13 m^2/g, see Figure S2 for X-ray diffraction and N_2-physisorption data), and to two commercial aluminium oxides, i.e. Al_2O_3 activated, neutral Brockmann I (particle size ~150 mesh, surface area: 155 m^2/g) and γ-Al_2O_3 nanopowder (particle size $<$50 nm, surface area: 171 m^2/g). The structure and textural properties of Al_2O_3-NR, e.g. surface area, nanorod morphology and presence of γ-Al_2O_3 phase are in line with our recent report (Figure S3 for selected characterisation data).[40] In this work, we improved the synthesis protocol of Ga_2O_3-NR, reaching a higher specific surface area (225 m^2/g) and tuning the size of the nanorods. TEM analysis confirmed that the material presents the rod-like morphology with length varying from 9 to 52 nm and width between 3 and 5 nm (Figure 1A). The X-ray diffractogram displays two major broad diffraction peaks at $2\theta = 35.54°$ and 61.92° (Figure 1B), which match well with the expected pattern attributed to the ε-Ga_2O_3 polymorph.[36] The N_2-adsorption-desorption isotherms of Ga_2O_3-NR can be classified as type II isotherms with H3 hysteresis loop over the relative pressure range of 0.62–0.97 (Figure 1C), attributed to the packing of the nanorods leading to the formation of slit-shaped interparticle voids. Additional characterisation data (FT-IR spectrum) can be found in the Supporting Information (Figure S4).

Initially, the Al and Ga oxides were screened as heterogeneous catalysts for the oxidation of aniline with 50 wt% aqueous hydrogen peroxide as the oxidant in an environmentally acceptable and inexpensive aprotic solvent as ethyl acetate (Table 1). In the absence of catalyst, almost no conversion of aniline was observed (Entry 1, Table 1). Among the tested Al and Ga oxides, the ε-Ga_2O_3 polymorph in the form of small nanorods (Ga_2O_3-NR) showed the highest aniline conversion (49% in 4 h, Table 1, Entry 7) with 92% selectivity towards azoxybenzene. Azobenzene, which is an industrially relevant molecule used in the production of dyes, food additives, pigments and therapeutic agents, was observed as the only side product.[5,41] This catalytic activity is markedly superior compared to that of Al_2O_3-NR and γ-Ga_2O_3, which showed moderate conversion of aniline (26 and 21%, respectively, see Entries 4 and 6 in Table 1), with azoxybenzene as the

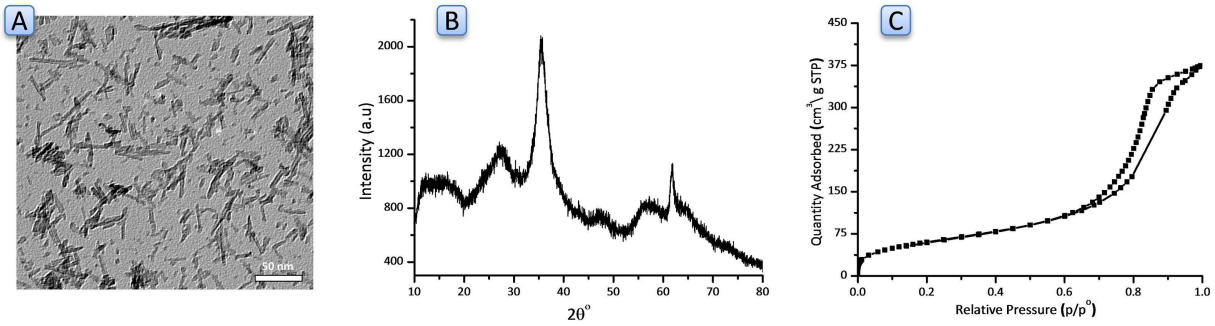
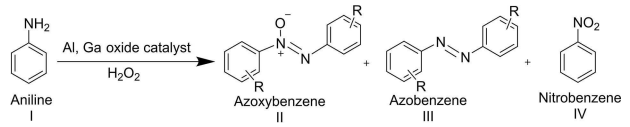


Figure 1. Characterisation of Ga_2O_3-NR: (A) TEM images, (B) XRD pattern, and (C) N_2 adsorption-desorption isotherms.

Table 1. Catalytic performance of Al and Ga oxides in the oxidation of aniline using 50 wt% aqueous H_2O_2.



Entry	Catalyst	Surface area [m^2/g]	Conv. [%] I	Sel. [%] II	III	IV
1	No catalyst	–	≤1	–	–	–
2	Al_2O_3 activated, neutral Brockmann I	155	11	28	34	39
3	Al_2O_3-nanopowder	171	14	38	37	25
4	Al_2O_3-NR	376	26	86	14	–
5	β-Ga_2O_3	13	≤1	–	–	–
6	γ-Ga_2O_3	155	21	98	2	–
7	Ga_2O_3-NR	225	49	92	8	–

Reaction conditions: aniline (2 mmol), anisole (1 mmol, as GC internal standard), 50 wt% H_2O_2 (4 mmol), catalyst (20 mg), ethyl acetate (4 g) as solvent, 80 °C, 4 h.

main product. On the other hand, both types of commercial Al_2O_3 (Table 1, Entry 2 and 3), displayed significantly lower activity and nitrobenzene was formed as a major product besides azoxybenzene and azobenzene, which indicates the further oxidation of the nitrosobenzene intermediate (Scheme 1). β-Ga_2O_3, which has the lowest surface area, was virtually inactive in this reaction (Table 1, Entry 5).

These differences in activity and selectivity can be correlated to the reaction mechanism, which involves both oxidation and condensation reactions (Scheme 1). The higher activity of Ga_2O_3-NR is attributed to the high, accessible surface area and to the large surface density of coordinatively unsaturated sites acting as acid sites that are able to activate hydrogen peroxide. Both features stem from the nanorod morphology of this material.[36] Previous work showed that Ga_2O_3-NR contains approximately 0.63 acid sites per nm^2.[36] With this figure in mind, the turnover number (TON) of Ga_2O_3-NR in the oxidation of aniline to azoxybenzene can be estimated to be 208. The differences in selectivity observed between the tested catalysts can be rationalised considering that the number and strength of Lewis and Brønsted acid sites on the surface of aluminium and gallium oxides depend not only on the intrinsic differences between the two metals, but also on the synthesis method of the materials, which determine surface area and morphology and thus also the surface density of accessible coordinatively unsaturated sites.[36,40] In this context, the higher selectivity towards nitrobenzene observed with the two commercial aluminas indicates that these materials are relatively poor in acid sites that are able to catalyse the condensation reaction between the reaction intermediates (phenylhydroxylamine and nitrosobenzene, see Scheme 1), which therefore tend to undergo further oxidation into nitrobenzene.

The catalytic performance of Ga_2O_3-NR in terms of activity and selectivity towards the desired products of the oxidation of aniline was further investigated as a function of reaction time (Figure 2). The conversion of aniline gradually increased, reaching 92% in 20 h, after which only a slight increase in aniline conversion was observed (94% in 26 h), suggesting the almost full consumption of hydrogen peroxide. This was confirmed by the negligible amount of H_2O_2 found in the reaction mixture after 26 h, as determined by titration with a 0.1 M Ce^{IV} solution. This indicates that a fraction of H_2O_2 disproportionated into H_2O and O_2. Based on these data, a 70% efficiency in the utilisation of H_2O_2 in the oxidation of aniline was achieved with the Ga_2O_3-NR catalyst. Azoxybenzene was the main product at all stages

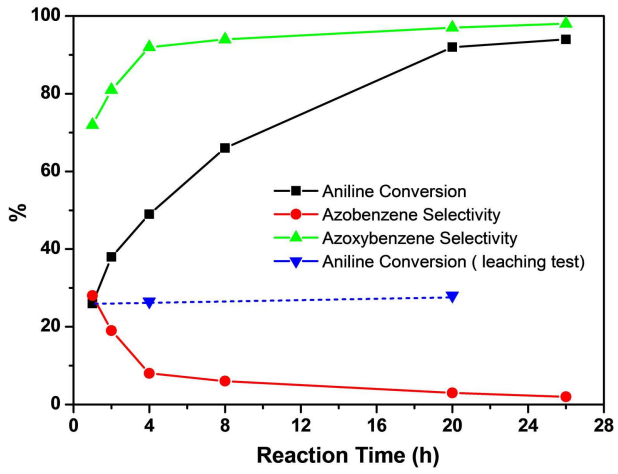


Figure 2. Conversion of aniline, selectivity towards azo and azoxybenzene, and leaching test with 50 wt% aqueous H_2O_2 as a function of reaction time over Ga_2O_3-NR. The reaction conditions are the same as those in Table 1.

of the reaction and its selectivity increased rapidly in the first 4 h of reaction, after which it slowly reached nearly full selectivity (98%) after 26 h. Remarkably, azobenzene was the only one side product and its selectivity decreased as a function of reaction time, suggesting the further oxidation of azobenzene to azoxybenzene (Scheme 1). No products of the over-oxidation of aniline such as nitrosobenzene and nitrobenzene were observed during the course of the reaction, whereas these side-products are commonly observed with transition-metal-containing catalysts.[3,21,22]

Besides achieving promising catalytic activity and selectivity, it is crucial to demonstrate the truly heterogeneous nature and the recyclability of the catalyst as these features are essential in view of possible industrial application. For this purpose, a hot filtration leaching test was performed (Figure 2, dotted line). The catalyst was removed by hot filtration after 1 h of reaction when the conversion of aniline was 26%. The filtrate was allowed to react for further 19 h reaching a final conversion of 28%. The very minor increase in aniline conversion after 20 h of reaction when compared to the 92% conversion obtained after 20 h in the presence of Ga_2O_3-NR (Figure 2) indicates that no or negligible leaching of active species occurred, proving the truly heterogeneous nature of the Ga_2O_3-NR catalyst. The recyclability of Ga_2O_3-NR was evaluated in several consecutive runs. The colour of Ga_2O_3-NR was slightly changed from white to light brown at the end of the first catalytic test, which indicates the adsorption of organic species on the surface of the catalyst. In order to remove these organic species, the catalyst was washed at 80 °C with ethyl acetate and ethanol. By following this procedure, the activity and selectivity of Ga_2O_3-NR were fully retained in four consecutive runs (Figure 3). This is in line with our previous results in the epoxidation of alkenes.[36]

The versatility of the Ga_2O_3-NR catalyst was tested in the oxidation of a range of substituted aromatic amines containing electron donor or acceptor groups on the phenyl ring (Table 2). Under the employed reaction conditions, most substituted amines were effectively and selectively ($\geq$92%) converted into the corresponding azoxy-derivatives (Entries 2–4 and 6, Table 2). The formation of the corresponding azo-derivatives was observed as the only minor side product. The behaviour was different when 4-methoxy aniline (*para*-anisidine) was used as substrate (Entry 5, Table 2). In such case, a 42% conversion was achieved but the main product was the azo-derivative (52% selectivity), with the other two products being the azoxy-derivative (38% selectivity) and 4-amino-4'-methoxydiphenyl amine (10% selectivity). The different selectivity in the conversion of 4-methoxy aniline compared to other substituted anilines can be ascribed to the increased electron density on the -NH_2 group in the 4-methoxy aniline due to the resonance effect of the methoxy group. For what concerns the trend in activity, the aromatic amines containing an electron donating group (Entries 2, 6, Table 2) or a weakly electron withdrawing group (Entry 3, Table 2) were more effectively converted into the corresponding azoxy-derivatives compared to those containing a strong electron withdrawing group as -NO_2 (Entry 4, Table 2). No steric effects were observed (compare Entry 1 and 6 in Table 2). It is worth noting that the open structure of Ga_2O_3-NR allows catalysing the conversion of bulky substrates, while a benchmark catalyst as TS-1 showed very poor activity in the conversion of 2-ethyl aniline due to diffusion limitations of this reactant in the micropores (d = 0.56 nm)[42] of the zeolite (compare Entries 6 and 7, Table 2).

With the purpose of fine-tuning the performance of the Ga_2O_3-NR catalyst, we investigated the effect of the catalyst loading, of the H_2O_2 source and of the amount of solvent on the conversion of aniline. The influence of the catalyst loading was studied over 5 mg, 10 mg, and 20 mg of Ga_2O_3-NR per mmol of aniline using 50 wt% aqueous H_2O_2 as the oxidant (Figure 4). The conversion of aniline and the selectivity towards azoxybenzene increase with the catalyst loading, reaching 70% aniline conversion with 94% azoxybenzene selectivity after 4 h reaction at 80 °C when employing 20 mg of Ga_2O_3-NR per mmol of aniline. Next, the effect of the H_2O_2 source was investigated. Hydrogen peroxide is commercially available in aqueous solution with different concentrations. The water supplied with the aqueous H_2O_2 and that formed during the reaction due to

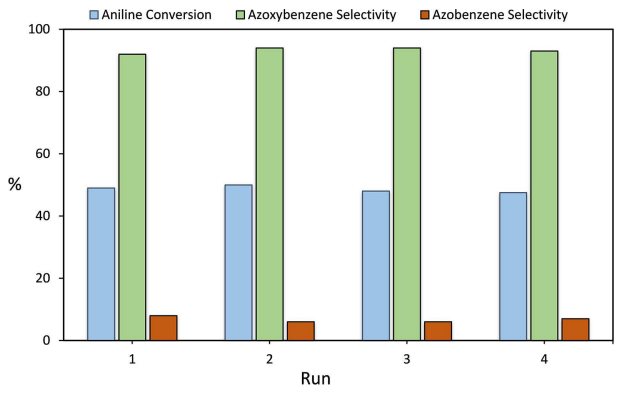


Figure 3. Recycling test of Ga_2O_3-NR as catalyst. Reaction conditions: aniline (2 mmol), anisole (1 mmol, as GC internal standard), 50 wt% H_2O_2 (4 mmol), Ga_2O_3-NR catalyst (20 mg), ethyl acetate (4 g) as solvent, 80 °C, 4 h.

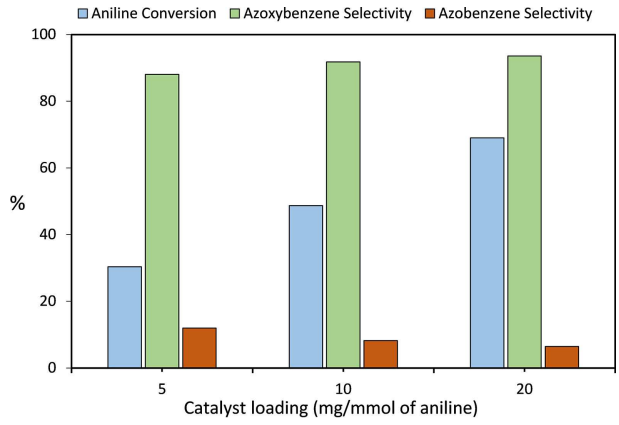
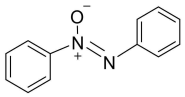
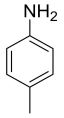
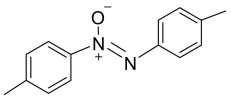
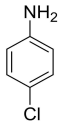
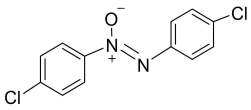
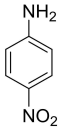
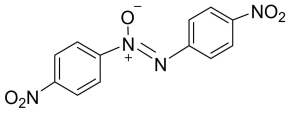
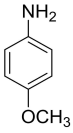
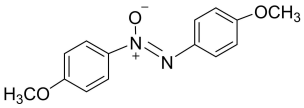
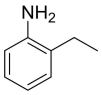
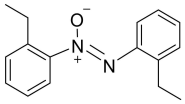
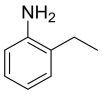
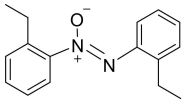


Figure 4. Influence of the Ga_2O_3-NR catalyst loading on the conversion of aniline and on the selectivity towards azo and azoxybenzene. Reaction conditions: 10 mg, 20 mg or 40 mg of Ga_2O_3-NR, aniline (2 mmol), anisole (1 mmol, as GC internal standard), 50 wt% H_2O_2 (4 mmol), ethyl acetate (4 g) as solvent, 80 °C, 4 h.

Table 2. Oxidation of aromatic amines into their azoxy derivatives with 50 wt% H_2O_2 catalysed by Ga_2O_3-NR.

Entry	Amines	Catalyst	Product (Substituted azoxybenzene)	Conv. [%]	Azoxy product Sel. [%]
1		Ga_2O_3-NR		49	92
2		Ga_2O_3-NR		58	96
3		Ga_2O_3-NR		54	97
4		Ga_2O_3-NR		22	93
5		Ga_2O_3-NR		42	38
6		Ga_2O_3-NR		49	95
7		TS-1		2	96

Reaction conditions: amine (2 mmol), anisole (GC internal standard, 1 mmol), 50 wt% aqueous H_2O_2 (4 mmol), catalyst (20 mg), ethyl acetate (4 g) as solvent, 4 h, 80 °C.

the utilisation or decomposition of H_2O_2, can influence the catalyst activity and selectivity. For example, it is well-documented that water is detrimental to the catalytic performance of Al_2O_3 in the liquid phase oxidation of alkenes with H_2O_2.[33,43–45] This effect has been attributed to the adsorption of H_2O on the catalyst surface, which hinders the access of H_2O_2 to the active sites. Considering the similarities between aluminium and gallium oxide,[36,45] it is worthwhile to investigate the influence of water on the oxidation of aniline over Ga_2O_3-NR. Therefore, we performed the oxidation of aniline by using three sources of H_2O_2: 50 wt% aqueous, 70 wt% aqueous, and 24.5 wt% of nearly anhydrous H_2O_2 in ethyl acetate (Figure 5). Significant improvement in the conversion of aniline and selectivity towards azoxybenzene were observed as a result of reducing the amount of water. The conversion of aniline increased from 49 to 62%, and the selectivity of azoxybenzene from 92 to 98%, by using 70 wt% aqueous H_2O_2 compared to 50 wt% aqueous H_2O_2. The catalytic performance did not improve further with the use of nearly anhydrous H_2O_2 in ethyl acetate, indicating that the Ga_2O_3-NR catalyst can operate efficiently also in the presence of some water.

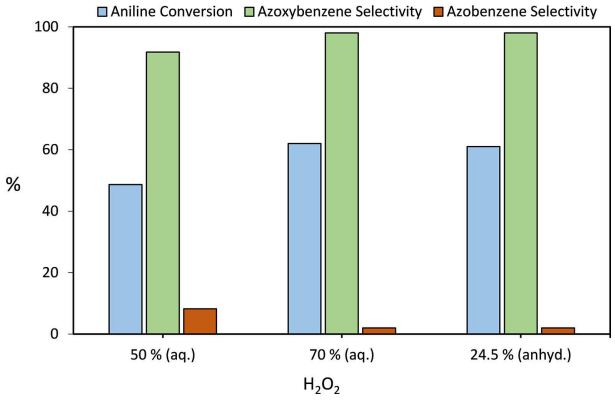


Figure 5. Influence of the hydrogen peroxide source on the conversion of aniline and on the selectivity towards azo and azoxybenzene over Ga_2O_3-NR. Reaction conditions: aniline (2 mmol), anisole (1 mmol, as GC internal standard), H_2O_2 (4 mmol), Ga_2O_3-NR catalyst (20 mg), ethyl acetate (4 g) as solvent, 80 °C, 4 h.

According to the principles of green chemistry, benign solvents or ideally no solvent should be employed in catalytic reactions. Besides ethyl acetate, which was selected as a green

solvent in analogy to previous studies of epoxidation reactions catalysed by Al_2O_3-NR[40] and Ga_2O_3-NR,[36] we tested dioxolane as alternative solvent but achieved lower activity and selectivity (Table S1). Further studies aimed at investigating if the reaction could be carried out with no or a minimum amount of solvent. This was studied with the Ga_2O_3-NR catalyst using 24.5 wt% anhydrous H_2O_2 (in ethyl acetate) as oxidant. Decreasing the amount of ethyl acetate led to a gradual increase in the conversion of aniline, while retaining very high selectivity towards azoxybenzene in all cases (Table 3). The conversion of aniline obtained without using extra solvent (93%, Entry 4, Table 3) was significantly higher compared to the reaction with the amount of ethyl acetate used in the rest of this work (Entry 1, Table 3). These results indicate that with the Ga_2O_3-NR catalyst the use of a solvent is detrimental, most likely as a consequence of a dilution effect that decreases the interaction between aniline and H_2O_2 on the surface of Ga_2O_3-NR. When considering the option of not adding a solvent, it should be taken into account that these experiments were carried out with anhydrous hydrogen peroxide, which forms a single liquid phase with aniline, whereas with aqueous hydrogen peroxide a biphasic liquid system would be formed with aniline in the absence of a solvent. In order to explore further the catalytic activity of Ga_2O_3-NR without adding a solvent, we tested the catalyst at lower temperature. Notably, Ga_2O_3-NR displayed significant activity also at 50 and even at 25 °C (Entry 4 and 5, Table 3), with only a minor decrease in selectivity towards azoxybenzene. Moreover, the activity and selectivity of the Ga_2O_3-NR were fully retained upon recycling also under these conditions (Entry 7, Table 3), in line with the results obtained with solvent (Figure 3).

Generally, the catalytic activation of hydrogen peroxide can occur through the formation of metal (hydro)peroxo species followed by heterolytic cleavage of the O–O bond, or follow a homolytic pathway involving the formation of hydroxyl radicals (•OH).[46] It has been extensively reported that the epoxidation of alkenes with H_2O_2 over Al_2O_2 or Ga_2O_3 catalysts proceeds through the formation of hydroperoxo species.[36,40,47] In order to gain more insight in the way in which Ga_2O_3-NR activates H_2O_2 towards the oxidation of aniline, a control experiment was performed in the presence of TEMPO (1 mol% to H_2O_2) as a radical scavenger. No difference was observed in the conversion of aniline and in the selectivity towards azoxybenzene with or without adding TEMPO (compare entry 5 and 8, Table 3). This result indicates that the catalytic mechanism over Ga_2O_3-NR does not involve radical species, thus ruling out homolytic cleavage of the peroxide bond. On the basis of these observations, a catalytic mechanism for the oxidation of aniline over Ga_2O_3-NR can be proposed (Scheme 2). Ga-OH groups located at the surface of the nanorods activate H_2O_2 through the formation of surface gallium hydroperoxide (Ga-OOH) species (steps 1 and 3), which are able to oxidise aniline to phenylhydroxylamine (step 2) and phenylhydroxylamine to nitrosobenzene (step 4) through heterolytic cleavage of the O–O bond. The acid sites at the surface of Ga_2O_3-NR are also expected to catalyse the subsequent formation of azoxybenzene through the condensation of the phenylhydroxylamine and nitrosobenzene intermediates (step 5).

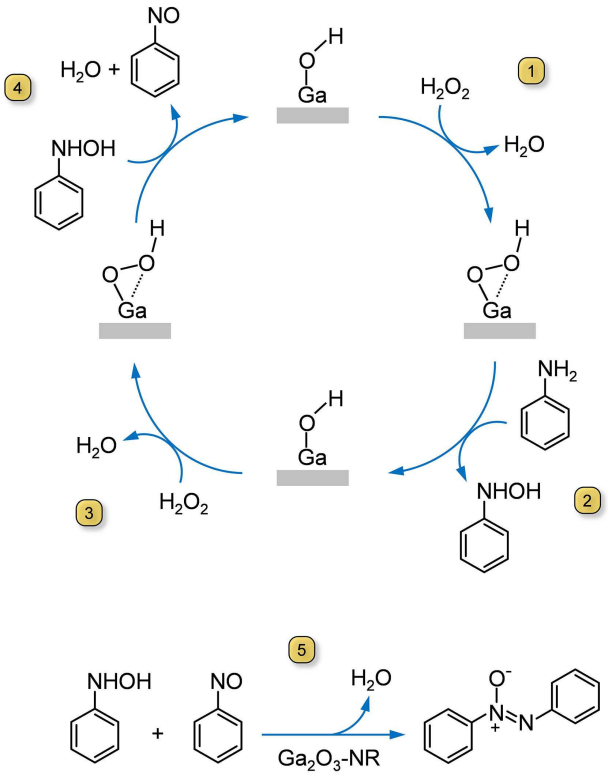
Table 3. Effect of solvent nature and amount on the conversion of aniline and selectivity towards azo and azoxybenzene with 24.5 wt% H_2O_2 (anhydrous, in ethyl acetate) over Ga_2O_3-NR.

Entry	Ethyl acetate [g]	T [°C]	Conv. [%]	Azobenzene Sel. [%]	Azoxybenzene Sel.[%]
1	4	80	61	2	98
2	2	80	63	2.2	98
3	1	80	69	1.9	98
4	No solvent	80	93	3	97
5	No solvent	50	47	4	96
6	No solvent	25	22	6	94
7[a]	No solvent	50	46	5	95
8[b]	No solvent	50	46	4	96

Reaction conditions: aniline (2 mmol), anisole (1 mmol) as GC internal standard, 24.5 wt% anhydrous H_2O_2 in ethyl acetate (4 mmol), Ga_2O_3-NR (20 mg), 4 h. [a] With reused catalyst. [b] In the presence of TEMPO (1 mol% relative to H_2O_2) as radical scavenger.

3. Conclusions

A set of Al and Ga oxides with different morphologies and crystal structures were studied as transition-metal-free heterogeneous catalysts for the oxidation of aromatic amines to azoxy derivatives using the environmentally friendly H_2O_2 as the



Scheme 2. Proposed catalytic cycle for the oxidation of aniline with H_2O_2 over Ga_2O_3-NR.

oxidant. Gallium oxide nanorods (Ga_2O_3-NR) displayed the most promising catalytic performance compared to the other transition-metal-free oxides, achieving 49% conversion of aniline with 92% selectivity towards azoxybenzene after 4 h of reaction at 80 °C, and reaching 94% conversion and nearly complete selectivity towards azoxybenzene (98%) at longer reaction times. The versatility of Ga_2O_3-NR was demonstrated in the conversion of substituted and bulky aromatic amines into their corresponding azoxy derivatives. Recycling tests demonstrated that the catalyst could be efficiently reused in consecutive catalytic cycles. The excellent catalytic results obtained with Ga_2O_3-NR are ascribed to the combination of high surface area, open structure and large surface density of coordinatively unsaturated sites acting as acid sites, which all stem from the nanorod morphology. Additionally, the activity of Ga_2O_3-NR could be substantially improved by using 70% aqueous or 24.5 wt% anhydrous hydrogen peroxide instead of 50% aqueous H_2O_2 as the oxidant and by minimising the amount of solvent used in the catalytic tests. Under these optimised conditions, Ga_2O_3-NR was active also under very mild conditions (25 or 50 °C). A test in the presence of a radical scavenger demonstrated that the reaction proceeds through the heterolytic cleavage of the activated peroxide species. In summary, this work introduces an effective and attractive catalytic system for the synthesis of (substituted) azoxy compounds and at the same time represents an advance in the exploration of the scope of applications of gallium oxide nanorods.[36,48]

Experimental Section

Materials

Anhydrous granular gallium chloride ($GaCl_3$, 99.999%) was purchased from Strem Chemicals Inc. Aluminium-tri-sec-butoxide ($Al(OBu^s)_3$, 97%), aniline (99.5%), anisole (99%), 50 wt% aqueous H_2O_2 were obtained from Sigma-Aldrich. The substituted anilines and 2-butanol (99%) were obtained from Acros Chemicals. Aqueous ammonia (25 wt%), ethanol, ethyl acetate (99.95%) were purchased from Boom chemicals. β-Ga_2O_3 (≥99.99% trace metal basis); γ-Al_2O_3 activated, neutral, Brockmann I; and γ-Al_2O_3 nanopowder were purchased from Sigma-Aldrich. 70 wt% aqueous H_2O_2 was provided by Peróxidos do Brasil (Solvay) in Brazil, for academic research. 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO, Sigma-Aldrich) was used as radical scavenger.

Catalyst Synthesis

Aluminium oxide nanorods (Al_2O_3-NR) were synthesised according to the protocol developed by some of us and reported in detail recently.[40] In a typical synthesis, aluminium tri-sec-butoxide (1.23 g, 5 mmol) was weighed in a 25 ml round bottle flask, then 2-butanol (1.60 g) was added dropwise within 10 min. The obtained clear solution was stirred for 30 min. After that, a solution of ammonium hydroxide (25 wt% aqueous) and absolute ethanol (1:1 v/v, 1.6 ml) was added dropwise over 30 min. The resulting white gel was stirred for 1.5 h and then heated at 70 °C for 23 h. Then, the obtained material was aged for 3 days at ambient temperature while stirring. Finally, the white precipitate was collected by centrifugation, thoroughly washed with absolute ethanol, and dried overnight in an oven at 80 °C in air. Finally, the powder was calcined in air at 400 °C for 10 h with a heating rate of 3 °C min^{-1}, leading to a typical yield of approximately 82%, assuming a product with Al_2O_3 formula.

Gallium oxide nanorods were prepared according to a modified version of a method previously reported by some of us.[36] This new protocol allows a precise control of the morphology and size of the nanorods, which is achieved by the adjustment of the addition of H_2O and 2-butanol. The required amount of anhydrous granular gallium chloride (99.999%) was weighed in a glove box under N_2 atmosphere because of its highly hygroscopic and deliquescent nature. In a typical synthesis, 4.80 g of 2-butanol were added dropwise using a pressure-equalising dropping funnel within 5 min into a 50 ml round bottom flask containing 15 mmol of gallium chloride under stirring at room temperature. As a result, a dark brown mixture was formed while HCl gas evolved. The mixture was stirred for 10 min and then 17.23 g of 2-butanol were added dropwise using a pressure-equalising dropping funnel over 30 min. The sample was stirred for further 1 h to obtain a mixture with a dark orange-brown colour. Next, a solution of 2.94 g of milli-Q water and 7.23 g of 2-butanol was added dropwise using a pressure-equalising dropping funnel over 1 h and stirred for 3 h at room temperature. Finally, the resulting mixture was stirred for 23 h at 70 °C and aged for 3 days at room temperature, yielding the gallium oxide nanorods in the form of a white solid precipitate. The obtained solid was separated by centrifugation (4500 rpm) and thoroughly washed with absolute ethanol (45 ml×5 times) and then dried at 80 °C for overnight. A typical yield of the gallium oxide nanorods was 18%, assuming a product with Ga_2O_3 formula.

γ-Ga_2O_3 was synthesised according to a procedure from the literature.[49] Briefly, 3.0 g of high-purity gallium nitrate (Strem Chemicals) were mixed in 50 ml of ethanol. Then, a solution of aqueous ammonia (25 wt%) diluted in ethanol (50 vol%) was added dropwise under continuous stirring at room temperature until no further precipitation was observed. The resulting precipitate was filtered, thoroughly washed with ethanol, and dried in vacuum at 60 °C for overnight. Finally, the white solid was calcined in air at 500 °C for 1 h with a heating rate of 3 °C min^{-1}, leading to a typical yield of approximately 96%, assuming a product with Ga_2O_3 formula.

Catalyst Characterisation

Powder X-ray diffraction (XRD) patterns were recorded on a Bruker D8 Advance diffractometer with a Cu Kα (λ = 0.15406 nm) radiation with a beam voltage of 40 kV and a beam current of 40 mA. The measurements were carried out in the region of 2θ = 10 to 80° with a scanning rate of 1.0°/min. The International Centre for Diffraction Data (ICDD) was employed to assign the XRD patterns. N_2-sorption experiments were performed using a Micromeritics ASAP-2020 instrument using N_2 as adsorbate at −196 °C. The Brunauer–Emmett–Teller (BET) method was used to calculate the specific surface area. Prior to the measurement, the samples were degassed under reduced pressure at 120 °C for 12 h (5 °C/min). Fourier transform infrared (FT-IR) spectra were measured on an IRTracer-100 spectrometer by averaging 32 scans with a spatial resolution of 4 cm^{-1}. Transmission electron microscopy (TEM) images were recorded on the Philips CM12 microscope operating at 120 kV. Prior to the measurement, the samples were suspended in ethanol by sonication for 5 min and then deposited onto a holey carbon film on a Cu grid.

Catalytic Tests

The catalytic tests for the conversion of aromatic amines into their azoxy derivatives were carried out in a 48-well parallel reaction block that allows the individual magnetic stirring of each well. In a typical reaction procedure, 20 mg of the catalyst, 4 g of ethyl acetate, and 4 mmol of aqueous hydrogen peroxide were mixed in a 10 ml glass vial. Then, a solution of 2 mmol of amine and 1 mmol of anisole as GC internal standard was added to the mixture. The obtained liquid was monophasic. The vials were capped with aluminium crimp seals with PTFE septa and placed each in a different position in the 48-well parallel reaction block. Then, each reaction mixture was stirred vigorously (900 rpm) at 80 °C for 4 h. Selected catalytic tests were performed in duplicate or in triplicate. In such cases, the average values for conversion and selectivity were reported (the standard deviation in the conversion of aniline and selectivity towards azoxybenzene was ±2%). Three types of hydrogen peroxide were employed in these tests (always using the same molar ratio between H_2O_2 and aniline): 50 wt% aqueous solution, 70 wt% aqueous solution and 24.5 wt% anhydrous in ethyl acetate. It should be noted that the concentration of hydrogen peroxide was almost the same (ca. 3 wt% of the reaction mixture) in all the catalytic tests. The catalytic tests with 70 wt% aqueous H_2O_2 were performed in Brazil. 24.5 wt% anhydrous H_2O_2 in ethyl acetate was prepared by removing water from the homogeneous solution of 20 ml of 50 or 70 wt% aqueous H_2O_2 and 188 ml of ethyl acetate by means of a Dean-Stark trap at 110 °C. Special attention should be dedicated to safety during this preparation, because anhydrous hydrogen peroxide in flammable organic solvents should be considered as dangerous and explosive.[50] Therefore, the preparation was carried out in a fume hood with a well ventilated preparation set-up in which the Dean-Stark trap was connected with a water condenser with open lid to release the oxygen generated by hydrogen peroxide decomposition and the possible explosive gas mixtures of solvent and oxygen. The concentration of H_2O_2 was determined by titration of the solution with a 0.1 M solution of $Ce(SO_4)_2$.

Conversion and selectivity were determined by gas chromatography (GC) on an Agilent 7890 B gas chromatograph, equipped with DB-5 fused silica column (15 m; 0.32 mm) and low thermal module (LTM) or on an Agilent 7890 A gas chromatograph, equipped with an HP 5 capillary column (30 m; 0.25 mm). The products were identified by comparison with standard solutions or by gas chromatography-mass spectroscopy analysis (GC-MS) on an Agilent Hewlett-Packard-HP 6890 gas chromatograph coupled with an Agilent Hewlett-Packard 5973 MSD mass spectrometer, equipped with Rxi®-5 Sil MS capillary column (30 m; 0.25 mm). Since 2 mol of amine are required for the formation of 1 mol of the corresponding azo and azoxy-derivatives, the conversion of aromatic amines and selectivity of azo and azoxy derivatives were calculated using the Equations (1) (2) (3):

$$\text{Conversion of amines } (\%) = [\text{mol of amine converted} / \text{initial mol of amine}] \times 100\,\% \quad (1)$$

where,

$$\text{mol of amines converted} = \text{initial mol of amine} - \text{mol of amine left after reaction} \quad (2)$$

$$\text{Selectivity towards azo or azoxy derivative } (\%) = [(2 \times \text{mol of azo or azoxy-derivative}) / \text{mol of amine converted}] \times 100\,\% \quad (3)$$

For the recycling tests, at the end of catalytic test, the reaction mixture was kept at room temperature for 30 min to allow the catalyst to settle down at the bottom of the glass vial. Then, most (90–95 vol.%) of the supernatant organic solution was removed using a pipette or a syringe. Next, 10 ml of ethyl acetate were added and the sample was stirred for 2 h at 80 °C. Then, the supernatant ethyl acetate was again removed and discarded after the catalyst settled at the bottom of the vial. This washing protocol was repeated again two times. Thereafter, the sample was transferred into a 50 ml centrifuge tube and dispersed in 40 ml of absolute ethanol. Then, the sample was centrifuged for 20 min at 4200 rpm to deposit the catalyst, after which the supernatant ethanol solution was removed. The washing procedure was repeated two times. Finally, the catalyst was dried overnight at 110 °C and reused for further catalytic tests. This washing protocol was repeated for each recycling test. All recyclability tests were performed in triplicate and average values for conversion and selectivity were reported (the standard deviation in the conversion of aniline and selectivity towards azoxybenzene was ±3%).

Leaching tests were performed under the general reaction conditions employed for the catalytic tests (vide supra). The catalyst was removed from the reaction mixture by centrifugation after 1 h reaction at 80 °C. A small aliquot of the filtrate was analysed by GC and the rest was allowed to react at 80 °C. An aliquot of the reaction solution was taken at the time intervals of 4 h and 20 h and analysed by GC.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: Transition-metal-free oxide · aniline oxidation · azoxybenzene · hydrogen peroxide · nanorods

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